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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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IMMUNEX CORPORATION
LAW DEPARTMENT
1201 AMGEN COURT WEST
SEATTLE, WA 98119

EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/001,848	CHIPMAN ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-21* is/are pending in the application.

4a) Of the above claim(s) *7-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 05/18/04 is acknowledged.

Claims 1 and 3-21 are pending.

Claims 7-21 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

Claims 1 and 3-6, drawn to a method of activating the immune system in a mammal comprising administering to the mammal an effective amount of an IMXP-888 polypeptide, wherein IMXP-888 polypeptide comprises an amino acid sequence of residues 18 to 375 of SEQ ID NO:3 or a polypeptide that is at least 80 % homologous to a polypeptide sequence that encodes residues 18 to 375 of SEQ ID NO:3 and under consideration in the instant application.

In view of the amendment, 05/18/04 the following rejections remain:

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 3-6 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a methods of *in vitro* (i) induction of secretion of specific cytokine , as disclosed in Table I of the current specification, from peripheral blood lymphocytes and (ii) calcium mobilization in various types of cells by soluble IMXP-888 polypeptide (SEQ ID NO:3) by does not reasonably provide **enablement** for (i) a method of activating the immune system in a mammal wherein the mammal wherein said mammal has various diseases, including viral infection , bacterial infection cancer or graft v host disorder, comprising administering to the mammal an effective amount of an IMXP-888 polypeptide, wherein IMXP-888 polypeptide comprises an amino acid sequence of residues 18 to 375 of SEQ ID NO:3 or a polypeptide that is at least 80 % homologous to a polypeptide sequence that encodes residues 18 to 375 of SEQ ID NO:3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim for the same reasons set forth in the previous Office Action, mailed 11/19/03.

Applicant's arguments, filed 05/18/04 have been fully considered, but have not been found convincing.

Applicant asserts that : (i) there is no strict requirement in paten law that in order to enable the claimed invention, actual clinical trials must be conducted; (ii) having identified a function of a sequences that at least 80% homologous to IMXP-888 polepetides that encodes residues 18 to 375 of SEQ ID NO:3, it is within the skill of those in the art to determine appropriate administration and dosage schedules; (iii) there in no evidence of record that the claimed invention would not work as intendent and hence, no rejection for lack of utility under 35 U.S.C. 101 has been made; (iv) one skilled in the art could without undue experimentation identify IMXP-888 polypeptides that are encoded by a sequence at least 80% homologous to IMXP-888 polepetides that encodes residues 18to 375 of SEQ ID NO:3 and which activate immune system.

Contrary to Applicant's assertions, the issue raised in the previous Office Action was not about requirement for actual clinical trials. In addition, Applicant is respectively remained that claims 1 and 3-6 were rejected under 35 U.S.C. 112, first paragraph not under 35 U.S.C. 101. As was stated previously, the specification only discloses detailed *in vitro* data of (i) induction of secretion of specific cytokine , as disclosed in Table I of the current specification, from peripheral blood lymphocytes by a soluble form of the murine protein FGFR β (see pages 23 – 24 of the current specification as filed) and (ii) calcium mobilization in various types of cells by a soluble form of the murine protein FGFR β (see pages25 and 26 of the current specification as filed). The specification does not adequately teach how to effectively activate the immune system in a mammal wherein said mammal has various diseases, including viral infection , bacterial infection cancer or graft v host disorder as recited in claim 2 by administering an effective amount of an IMXP-888 polypeptide wherein IMXP-888 polypeptide comprises an amino acid sequence of residues 18 to 375 of SEQ ID NO:3 or a polypeptide that is at least 80 % homologous to a polypeptide sequence that encodes residues 18 to 375 of SEQ ID NO:3.
It was also stated that it is not clear that reliance on the *in vitro* data accurately reflects the relative mammal and human efficacy of the claimed therapeutic strategy. The specification does not teach how to extrapolate data obtained from *in vitro* studies to the development of effective *in vivo* mammalian including human therapeutic treatment, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of activating the immune system in a mammal wherein said mammal has various diseases, including viral infection , bacterial infection cancer or graft v host disorder as recited in claim 2 by administering an effective amount of an IMXP-888 polypeptide wherein IMXP-888 polypeptide comprises an amino acid sequence of residues 18 to 375 of SEQ ID NO:3 or a polypeptide that is at least 80 % homologous to a polypeptide sequence that encodes residues 18 to 375 of SEQ ID NO:3. Moreover, Applicant himself acknowledge that the contrary to expectations, no direst proliferation effects of IMXP-888 were observed in any of the cell types tested. (see page 1, lines 30-35 of the Specification as filed) . As such, the invention must be considered unpredictable. There was no requirement for a clinical studies , however, in the absence of *in vivo* working examples, the intended *in vivo* uses of an IMXP-888 polypeptide

wherein IMXP-888 polypeptide comprises an amino acid sequence of residues 18 to 375 of SEQ ID NO:3 or a polypeptide that is at least 80 % homologous to a polypeptide sequence that encodes residues 18 to 375 of SEQ ID NO:3 in a method of activating the immune response are fraught with uncertainties.
Moreover, an effective protocol for a method of activating the immune system, is subject to a number of factors which enter the picture beyond simply the administration to the subject an effective amount of an IMXP-888 polypeptide wherein IMXP-888 polypeptide comprises an amino acid sequence of residues 18 to 375 of SEQ ID NO:3 or a polypeptide that is at least 80 % homologous to a polypeptide sequence that encodes residues 18 to 375 of SEQ ID NO:3. Demonstrating *in vitro* data of (i) induction of secretion of specific cytokine , as disclosed in Table I of the current specification, from peripheral blood lymphocytes by a soluble form of the murine protein FGFR β (see pages 23 –24 of the current specification as filed) and (ii) calcium mobilization in various types of cells by a soluble form of the murine protein FGFR β (see pages25 and 26 of the current specification as filed) cannot alone support the predictability of a method of activating the immune system in a mammal wherein said mammal has various diseases, including viral infection , bacterial infection cancer or graft v host disorder by administering an effective amount of an IMXP-888 polypeptide wherein IMXP-888 polypeptide comprises an amino acid sequence of residues 18 to 375 of SEQ ID NO:3 or a polypeptide that is at least 80 % homologous to a polypeptide sequence that encodes residues 18 to 375 of SEQ ID NO:3. Van Noort et al. (International Review of Cytology, 1998) indicate factors that effect immune response such as genetic, environmental and hormonal (Page 176, Paragraph 3). The ability of a host to enhance an immune response will vary depending upon factors such as the condition of the host and burden of disease. Treatment/administration protocols depend upon the nature of the compound being administered as well as the clinical condition of the subject or patient. In the absence of additional information the skilled artisan would not have been able to use the undisclosed compound for activating the immune response without undue experimentation.

With regards to the issues that it is within the skill of those in the art to determine appropriate administration and dosage schedules and that one skilled in the art could without undue experimentation identify IMXP-888 polypeptides that are encoded by a sequence at least 80% homologous to IMXP-888 polepetides that encodes residues 18to 375 of SEQ ID NO:3 and which activate immune system.

Contrary to Applicant's assertion, Applicant has not taught how to make any polypeptide that is at least 80% homologues to a polypeptide sequence that encodes residues 18 to 375 of SEQ ID NO:3 to be used in the method of activating the immune system in a mammal in need. The structural and functional characteristics of said peptides are not defined in the claim, the specification fails to provide sufficient guidance as to which core structure of SEQ ID NO: 3 is essential activating the immune system in a mammal in need and which changes can be made in the structure of SEQ ID NO: 3 and still maintained the same function. Applicant is relying upon certain biological activities and the disclosure of a single species to support an entire genus. The

claims as written encompass a broad genus of polypeptides that at least 80% homologues to a polypeptide sequence that encodes residues 18 to 375 of SEQ ID NO:3 with an unlimited number of possibilities with regard to the length of the polypeptide sequence. Further, the enablement issues of making the protein still remain because the specification does not teach and provide sufficient guidance as to which amino acid of SEQ ID NO:3 would have been altered such that the resultant polypeptide would have retained the function of activating the immune system. Therefore, absent the ability to predict which of these peptides would function as claimed, and given the lack of data on regions critical for activity, for one of skill in the art to practice the invention as claimed would require a level of experimentation that is excessive and undue.

Since the instant fact pattern fails to indicate that representative number of structurally related compounds is disclosed, the artisan would not know the identity of a reasonable number of representative compounds falling within the scope of the instant claims and consequently would not know how to make them. An assay for *finding* a product is not equivalent to a positive recitation of *how to make* a product.

Consequently, without additional guidance in the specification, and the dearth of information in the art, for one of skill in the art to practice the invention as claimed, would require experimentation that is excessive and undue. The amount of guidance or direction needed to enable an invention is inversely related to the mount of knowledge in the state of the art as well as the predictability in the art (In re Fisher, 427 F.2d 833, 839, 166 USPQ 18,24 (CCPA 1970)).

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed method of activating the immune system in mammals wherein said mammal has various diseases, including viral infection , bacterial infection cancer or graft v host disorder comprising administering an effective amount of an IMXP-888 polypeptide wherein IMXP-888 polypeptide comprises an amino acid sequence of residues 18 to 375 of SEQ ID NO:3 or a polypeptide that is at least 80 % homologous to a polypeptide sequence that encodes residues 18 to 375 of SEQ ID NO:3 in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

3. Claims 1and 3-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action, mailed 11/19/03.

Applicant's arguments, filed 05/18/04 have been fully considered, but have not been found convincing.

Applicant asserts that it is not necessary to disclosed all the embodiments of the invention and that the specification describes several examples of IMXP-888 polypeptides within the recited scope and describes how to test additional IMXP-888 polypeptides .

Contrary to Applicant's assertion, a description of a protein by functional language in the absence of a structure is not considered sufficient to show possession of the claimed invention. See Fiers, 984 F.2d at 1169-71, 25 USPQ2D at 1605-06. It is only a definition of a useful result rather than a definition of what achieves that result. Many species may achieve that result. The definition requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 /f.2d 1516, 1521, 22 USPQ 369, 372-73 (Fed. Cir. 1984) affirming the rejection because the specification does "little more than outline[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what the material consists of (e.g. structural feature), is not a description of that material.

Applicant is not in possession of : a method of activating the immune system in a mammal wherein said mammal has various diseases, including viral infection , bacterial infection cancer or graft v host disorder comprising administering to the mammal an effective amount of an IMXP-888 polypeptide, wherein IMXP-888 polypeptide comprises an amino acid sequence of residues 18 to 375 of SEQ ID NO:3 or a polypeptide that is at least 80 % homologous to a polypeptide sequence that encodes residues 18 to 375 of SEQ ID NO:3.

The specification fails to define all a polypeptide that is at least 80 % homologous to a polypeptide sequence that encodes residues 18 to 375 of SEQ ID NO:3 that can be used in a method of activating the immune system in a mammal wherein said mammal has various diseases, including viral infection , bacterial infection cancer or graft v host disorder. The lack of sufficient limitations would therefore allow for all IMXP-888. Applicant has disclosed a limited number of species; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of

the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

Neither the exemplary embodiments nor the specification's general method appears to describe structural features, in structural terms, that are common to the genus. That is, the specification provides neither a representative number of species of a polypeptide that is at least 80 % homologous to a polypeptide sequence that encodes residues 18 to 375 of SEQ ID NO:3 that can be used in a method of activating the immune system in a mammal to describe the claimed genus, nor does it provide a description of structural features that are common to species. As discussed above, the specification provides no structural description of any polypeptide that is at least 80 % homologous to a polypeptide sequence that encodes residues 18 to 375 of SEQ ID NO:3 that can be used in a method of activating the immune system in a mammal other than ones specifically exemplified; in essence, the specification simply directs those skilled in the art to go figure out for themselves what the claimed polypeptide looks like. The specification's disclosure is inadequate to describe the claimed genus of any polypeptide that is at least 80 % homologous to a polypeptide sequence that encodes residues 18 to 375 of SEQ ID NO:3 that can be used in a method of activating the immune system in a mammal.

A description of what a material does rather than of what it is, usually does not suffice. The patent does not more than describe the desired function of the compound called for and contains no information by which a person of ordinary skill in the art would understand that the inventors possessed the claimed invention. At best, it simply indicates that one should run tests on a wide spectrum of compounds in the hope that at least one of them will work. Inadequate written description that merely identifies a plan to accomplish an intended result "is an attempt to preempt the future before it has arrived" *Fiers v. Revel*, 984 F.2d 1164,1171 9Fed.Cir. 1993).

A description of a genus of protein sequences may be achieved by means of a recitation of a representative number of polypeptide sequences, defined by amino acid sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The following new ground of rejection are necessitated by the amendment filed 05/18/04

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claim 1, 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent Publication 2002/0197674, or WO 01/70977 or by WO 01/00673 each in view of US Paten 5,807,862.

Applicant asserts that: US '674 does not teach or suggest each and every limitation of the claimed invention; WO'977 does not teach activating the immune system in a mammal with viral infection; WO'673 does not indicate whether one should use MANGO 003 to treat any particular disease, for example viral infection; US '862 does not teach or suggest using IMXP-888 to activate the immune system to treat viral infection.

Applicants have traversed the primary and the secondary references pointing to the differences between the claims and the disclosure in each reference. Applicant is respectfully reminded that the rejection is under 35 USC103 and that unobviousness cannot be established by attacking the references individually when the rejection is based on the combination of the references. see In re Keller, 642 F.2d 4B, 208 USPQ 871, 882 (CCPA 1981) See MPEP 2145. This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968).

US Patent Publication '674 teaches a method of activating biological function in mammals, including immune response, comprising administering into the mammal an effective amount of PRO943 polypeptide or a polypeptide encoding by a sequence that is at least 80 % homologues to PRO943 polypeptide . (see entire document, Abstract, , column 41, column 169 , in particular). US Patent '674 teaches that PRO943 polypeptide is glycosylated (see column 199 in paricular). It is noted that PRO093 polypeptide is 100 % identical to the claimed IMXP-888 polypeptides of SEQ ID NO:3 (see attached sequence alignment) .

WO'977 teaches a method of treatment of diseases in mammals, including method of activation immune response, comprising administering into the mammal an effective amount of FGFR polypeptide or a polypeptide encoding by a sequence that is at least 80 % homologues to FGFR polypeptide . (see entire document, Abstract, pages 27, 60, 76, 77,in particular). WO'977 teaches that FGFR polypeptide is glycosylated (see page 37 in particular). It is noted that FGFR polypeptide is 100 % identical to the claimed IMXP-888 polypeptides of SEQ ID NO:3 (see attached sequence alignment) .

WO'673 teaches a method of treatment of diseases in mammals, including method of activation immune response, comprising administering into the mammal an effective amount of MANGO 003 polypeptide or a polypeptide encoding by a sequence that is at least 80 % homologues to FGFR polypeptide . (see entire document, Abstract, pages 5, 29 and 76 in particular). WO'673 teaches that MANGO 003 polypeptide is glycosylated (see page 30 in particular). It is noted that MANGO 003 polypeptide is 100 % identical to the claimed IMXP-888 polypeptides of SEQ ID NO:3 (see attached sequence alignment) .

US Patent Publication 2002/0197674, or WO 01/70977 or by WO 01/00673 do not teach a method of activating the immune system in a mammal, wherein the mammal has viral infection.

US Patent 5,807862 teaches a method of treating a number of diseases, including viral infection, in mammals including humans, by stimulating immune system in response to FGF administration (see entire document, overlapping column 12 and 13 in particular).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of US Patent 5,807862 to those of US Patent Publication 2002/0197674, or WO 01/70977 or by WO 01/00673 to obtain a claimed method of activating the immune system in a mammal, wherein said mammal has viral infection, comprising administering to the mammal an effective amount of an IMXP-888 polypeptide.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because viral infection can be treated by activating the immune system as taught by US Patent 5,807862. This can be used in the method taught by US Patent Publication 2002/0197674, or WO 01/70977 or by WO 01/00673 of activating the immune system in a mammal, wherein said mammal has viral infection, comprising administering to the mammal an effective amount of an IMXP-888 polypeptide. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of

reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

Claim 3 in included because human is an obvious species of mammal genus. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use IMXP-888 polypeptide in a method of activating the immune system in a mammal, wherein the mammal is human as taught by 2002/0197674, or WO 01/70977 or WO 01/00673. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary

6. No claim is allowed.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840 The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
June 22, 2004

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600